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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
09/020,743	02/09/98	MACK	D	018547-03480

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EXAMINER
SIEW, J

ART UNIT	PAPER NUMBER
1634	6

DATE MAILED: 03/05/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/020,743	Applicant(s) Mack
	Examiner Jeffrey Siew	Group Art Unit 1634

☐ Responsive to communication(s) filed on _____ .

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire ____3____ month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-48* _____ is/are pending in the application.

    Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-48* _____ is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

    ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

        ☐ received.

        ☐ received in Application No. (Series Code/Serial Number) _____ .

        ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

    *Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *5 (2 pgs)*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- *SEE OFFICE ACTION ON THE FOLLOWING PAGES* ---

DETAILED ACTION

Drawings

1.   This application has been filed with informal drawings which are acceptable for

examination purposes only. Formal drawings will be required when the application is allowed.

Specification

2.   The title of the invention is not descriptive. A new title is required that is clearly indicative

of the invention to which the claims are directed.

The following title is suggested: Computer-aided display for Comparative Gene

Expression

Claim Rejections - 35 USC § 112

3.   The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and
> distinctly claiming the subject matter which the applicant regards as his invention.

4.   Claims 1-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A)   Claims 1-48 are confusing because it cannot be determined whether the two axis are connected.

B)   Claims 1-48 are vague and indefinite because of the terms "position" and "relative" in claims 1,20,25,44,47 & 48. It cannot be determined what measure is used to define the meaning of "relative". It is suggested that position be amended to "position with X,Y coordinates where in the X position is selected relative to the first axis and Y axis etc". For subsequent claims 19 & 43 which involve a third axis, it is suggested to add Z coordinates. The use of these terms would have been well known and commonly practiced in the art of graphically displaying images.

C)   Claims 1-48 are vague and indefinite because of the term "corresponding". Particularly in claims 1,20,25,44,47 & 48, it cannot be determined in what way or manner the "correspondence" is to occur.

D)   Claim 4 recites the language "mark step" and depends on claim 1. However, proper

antecedent basis is lacking in claim 1.Claim 4 depends on claim 1 which recites the language of

"displaying a mark". However, claim 1 does not recite a "mark step". It cannot be determined

what the term is referring to.

E)   Claim 6 recites the language " said monitoring step" and depends on claim 3. However,

proper antecedent basis is lacking in claim 3. It cannot be determined to what monitoring step is

being referred to.

F)   Claim 25 recites the language "first and second". However, proper antecedent basis is

lacking in claim 25 for these terms. It is suggested the claims be amended to include "a first and

second".

G)   Claim 6-10 are confusing because it cannot be determined to where the step of inputting is

to occur. It cannot be determined whether the input is referring to the probe pair into the samples

or the results into a computer for display.

H)　　Claim 6 is confusing because it cannot be determined at what point the steps are to be performed in relationship to the steps in claims 1 & 6. It is suggested that a phrase be included in the preamble reciting "wherein the comparing step" further comprises".

I)　　Claim 10 & 34 are confusing because of the term "pairs that cause" because it cannot be determined as to what the pairs are to cause.

J)　　Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: computing the IDIF between the Ipm-Imm. Clarificaton is requested.

K)　　Claim 10 &34 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: averaging the IDEF values. The specification discloses that the determination of expression is based on several calculations may be used to calculate the expression level (see page 11, lines 5-14). However in using the calculation of the sum of IDEF values as recited in claim 10 would necessitate an averaging step.

L)   Claim 11 & 35 are confusing because of the phrase "user input selecting said mark" is not grammatically correct. It cannot be determined what the phrase is referring to. It is suggested the phrase be amended to " an input of a user's selection of said mark".

M)   Claims 11,12 & 36 are confusing because of the term "information". It cannot be determined to what or what type of information is to be displayed. The rejection would be overcome if the claims were to be amended to include "comprises a GENBANK accession number".

N)   Claim 17 & 41 are confusing because it cannot be determined " treatment strategy". It cannot be determined how a characteristic comprises a " treatment strategy".

O)   Claims 16 & 40 are confusing because of the phrase "presence of disease". Although disease level or state are commonly used, the use of "presence" would more likely refer to an actual physical presence such as a bacteria or virus. It is suggested that the claim be amended to "disease state".

P)   Claim 30 recites the language " said monitoring step" and depends on claim 3. However, proper antecedent basis is lacking in claim 27. It cannot be determined to what monitoring step is being referred to.

Claim Rejections - 35 USC § 102

5.   The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the

basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6.   Claims 1-4, 19-21 & 24 are rejected under 35 U.S.C. 102(b) as being Guo et al by (NAR

vol. 22, No. 24 1994).

Claims 1-4,19-21 & 24 are drawn to displaying expression levels of two samples on a

graph in which the first axis corresponds to expression level of first sample and the second axis is

perpendicular to first axis and corresponds to expression level of second sample and a mark is

displayed.

Guo et al use oligonucleotide array to detect differences in mutations between wild types

and several mutants. He displays the results in a 3 D graph in which the axis each correspond to

the presence of targeted sequence in five different samples (see Figure 5).

Claim Rejections - 35 USC § 103

7.   The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness

rejections set forth in this Office action:

> (a) a patent may not be obtained though the invention is not identically disclosed or described as set forth in
> section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are
> such that the subject matter as a whole would have been obvious at the time the invention was made to a person
> having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the
> manner in which the invention was made.

8.   Claims 1-18,23 & 25-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over

Lockhart et al (WO97/27317 21 July 1997).

Claims 1-18 are drawn to claim 1 in which the expression level of expressed sequence is

monitored.

Claims 25-43 are drawn to computer product comprising code for displaying a first axis

corresponding to expression level of first axis, code for displaying a first axis corresponding to

expression level of first axis and code for displaying a mark , a computer readable storage medium

for storing codes.

Claims 44-46 are drawn to drawn to computer product comprising code for displaying a

first axis corresponding to a compound concentration, code for displaying a first axis

corresponding to compound concentration and code for displaying a mark , a computer readable

storage medium for storing codes.

Claim 47 is drawn to computer system comprising code for displaying a first axis

corresponding to expression level of first axis, code for displaying a first axis corresponding to

expression level of first axis and code for displaying a mark , a computer readable storage medium

for storing codes.

Claims 48 is drawn to computer system comprising code for displaying a first axis

corresponding to a compound concentration, code for displaying a first axis corresponding to

compound concentration and code for displaying a mark , a computer readable storage medium

for storing codes.

Lockhart et al teach a method of detecting nucleic abundances or concentrations (e.g.

expression levels) between two or more samples (see whole document esp. abstract). They teach

the simultaneous monitoring of the expression of a multiplicity of genes using perfect match probe

and mismatch probes (see page 5,12,47 & esp. 49-50). They teach that expression monitoring

would be useful for both drug safety and toxicology screenings (see page 230) and monitoring

various genes in response to defined stimuli such as drugs (see page 22). They teach that

monitoring of gene expression may be performed using a computer system running a software

program that includes computer code incorporating analysis of hydridization intensities of the

screens(see page 90 & Figure 6-8). They teach a method of comparing expression level using the

hybridization intensities between the perfect match and mismatch probes (see page 93-101 &

Figure 9-10B). They compare the hybridization intensity difference and ratio of the perfect match

and mismatch probes with a threshold. The values NPOS, NNEG and LR are calculated for each

pair of probes. The analysis is repeated to calculate the average of the differences. They teach that oligonucleotide pairs that show the greatest differential hybridization between two samples can be identified by sorting the observed hybridization ratio and difference values. Based on identified oligonucleotide pair sequences, a gene can be searched for in sequence databases such as GENBANK (see page 128-9). They also display the results in a graph showing differential expression between samples (see Figures 16-17).

Lockhart et al do not teach the displaying the expression level information comprising displaying a first axis corresponding to expression level in a first sample, displaying second axis in second sample, displaying a mark at a position relative to first axis according to expression level in first sample and relative to second axis according to expression level in second sample.

One of ordinary skill in the art would have been motivated to display the gene expression of two samples in Lockhart et al's analysis technique on a single graph in order to compare the gene expression between two different samples. Lockhart et al state that their method is particularly useful in comparing the gene expression of two different samples especially in drug screening and toxicology studies. It was well known and commonly practiced in the art to construct graphs with an different axis each representing different scales to analyze the data in relationship between parameters. It would have been prima facie obvious to construct a graph with an x axis representing the gene expression in one sample and the y axis representing the gene expression in a second sample and a even a third axis representing the gene expression in a third sample in order to compare the differential gene expression between the different samples.

9. Claims 22 & 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lockhart

et al (WO97/27317 21 July 1997) in view of Beattie (US5,843,767 December 1, 1998).

Claims 22 & 24 are drawn to claim 20 with the added limitation the polymer is a protein.

The teachings and suggestions of Lockhart et al are described above.

Lockhart et al does not teach the use of protein polymers.

Beattie et al teach the use of protein probes such as antibodies in hybridization array (see

whole document).

One of ordinary skill in the art would have been motivated to apply Beattie et al's teaching

of using protein probes to Lockhart et al's expression display in order to compare the expression

level of actual translated protein between two samples. Beattie states that the use of antibodies or

ligand receptor binding would be applicable to the study of identifying biomolecules. It was well

known and commonly practiced to use these ligand -receptor binding techniques in order to

actually identify the stage of gene expression i.e. the translated protein. It would have been prima

facie obvious to use Beattie's protein probes and display the results between two samples using

Lockhart et al's expression method in order to compare the protein levels which represent the

final stage of gene expression.

10. Any inquiry concerning this communication or earlier communications from the examiner

should be directed to Jeffrey Siew whose telephone number is (703) 305-3886 and whose e-mail

address is jsiew@uspto.gov. The examiner can normally be reached on Monday through Friday

from 6:30 a.m. to 3 p.m. If attempts to reach the examiner by telephone are unsuccessful, the

examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application or proceeding

should be directed to the receptionist for Technology Center 1600 whose telephone number is

(703) 308-0196.

Papers related to this application may be submitted to Group 1600 by facsimile

transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal

Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette,

1096 OG 30 (November 15, 1989). The CM1 Center numbers for Group 1600 are Voice (703)

308-3290 and Fax (703) 305-3014 or (703) 305-4242.
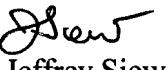
Jeffrey Siew

February 26, 1999

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600

3/1/99